

REJECTION UNDER 35 U.S.C. §101

Claims 1-3 stand rejected under 35 U.S.C. §101 for allegedly lacking either a specific and substantial asserted utility, or a well established utility.

Applicants assert that their identification of SP168 receptor ligands is useful in that these ligands permit methods for identifying SP168 receptor agonists and antagonists that would be useful for treating SP168-receptor related medical conditions (see, *e.g.*, page 2, lines 9-14). Applicants exemplified specific medical conditions that appear to be linked to the expression of SP168 receptor in human brain and spinal tissue (see, *e.g.*, page 2, lines 1-7). Such medical conditions include, neurodegenerative disorders such as Parkinson's, Alzheimer's, Huntington's, amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS) (see, *e.g.*, page 2, lines 4-7). Furthermore, Applicants demonstrated by *in situ* hybridization that disease-related tissue tended to exhibit lower hybridization signals for SP168 than did normal tissues (see, *e.g.*, page 29, lines 30-36). Consequently, Applicants demonstrated a nexus between expression of SP168 receptor and specific medical conditions. As such, Applicants contend that the presently claimed invention has a specific and substantial utility that is credible.

Ji et al. describe the general structure of G protein-coupled receptors. In addition, *Ji et al.* describe the diversity of ligand binding and receptor activation found among G protein-coupled receptors. As pointed out by the Examiner, *Ji et al.* indicate that G protein coupled receptors "are classified into over 100 subfamilies according to sequence homology, ligand structure, and receptor function" (see *Ji et al.*, page 17299, column 1, paragraph 1, line 2). *Ji et al.* also indicate that "a substantial degree of amino acid homology is found among members of a particular subfamily of G protein-coupled receptors, but comparisons between subfamilies show significantly less or no similarity" (see *Ji et al.*, page 17299, column 1, paragraph 1, line 3). Thus, based on *Ji et al.*, a skilled artisan would not only be able to identify the SP168 receptor as a G protein-coupled receptor but may further classify it into a subclass. In fact, based on SP168 receptor's pharmacological properties, this G protein-coupled receptor was further classified by Applicants into the subclass of P2Y receptors (see, *e.g.*, page 4, lines 23-25).

Ji et al. further point out that:

Mutations [of G protein-coupled receptors] have been observed that relate to a wide spectrum of hereditary and somatic disorders and diseases from cancer to infertility. These mutant receptors are incapable of binding ligand or generating normal signals, constitutively generate signals, or are not appropriately expressed on the cell surface.

(See Ji *et al.*, page 17299, column 1, paragraph 2, lines 1-2). Thus, one of skill in the art could readily appreciate that, as SP168 receptor is a G protein-coupled receptor, disorders and diseases related to the expression of SP168 receptor are likely.

Hollopeter *et al.* describe a polypeptide that shares 100% sequence homology with SP168 receptor. Like Applicants of the present invention, Hollopeter *et al.* recognize this polypeptide as being a G protein-coupled receptor whose ligand is ADP and likewise classify it as a P2Y receptor. Hollopeter *et al.* point out that they “found selective expression [of this G protein-coupled receptor] in platelets and brain in rat tissues (data not shown)” (see Hollopeter *et al.*, page 204, column 2, paragraph 1, line 3). Hollopeter *et al.* provide evidence that this G protein-coupled receptor is involved in ADP-dependent platelet aggregation and is targeted by antithrombotic drugs (see, Hollopeter *et al.*, page 206, column 1, paragraph 2). Nowhere do Hollopeter *et al.* provide any evidence that this polypeptide is not involved in neurodegenerative disorders as asserted by Applicants.

In conclusion, based on the specific, substantial, and credible utility asserted above, Applicants respectfully request withdrawal of this rejection.

REJECTIONS UNDER 35 U.S.C. § 112

Based on the above rejection, Claims 1-3 stand rejected under 35 U.S.C. 112, first paragraph for allegedly not providing sufficient guidance to one skilled in the art on how to use the claimed invention to identify agonists or antagonists of SP168 receptor.

As described above, Applicants assert that their identification of SP168 receptor ligands is useful in that these ligands permit methods for identifying SP168 receptor agonists and antagonists that would be useful for treating SP168-receptor related medical conditions (see, *e.g.*, page 2, lines 9-14). Such medical conditions include, neurodegenerative disorders such as Parkinson’s, Alzheimer’s, Huntington’s, amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS) (see, *e.g.*, page 2, lines 4-7). As discussed above, Applicants contend that the presently claimed invention has a specific and substantial utility that is credible.

Contrary to the Examiner’s position, methods for identifying agonists and antagonists of SP168 receptor are routine to one skilled in the art and do not require undue experimentation. In addition, Applicants provide more than sufficient guidance to one skilled in the art. See, *e.g.*, specification, page 25, line 13 to page 28, line 13. Notably, Applicants have identified twelve agonists and two antagonists of the SP168 receptor using the screening assays disclosed (see, *e.g.*, page 25, lines 19-20 and lines 27-28, respectively).

Based on the specific, substantial, and credible utility asserted above, as well as the guidance to one skilled in the art on how to use the present invention, Applicants respectfully request withdrawal of this rejection.

Claims 1-3 stand rejected under 35 U.S.C. 112, first paragraph for allegedly lacking enablement. See section below for a discussion regarding both enablement and written description.

Claims 1 and 2 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking sufficient written description to reasonably convey to one skilled in the art that at the time the application was filed the inventors had possession of the claimed invention.

As pointed out by the Examiner, “the specification discloses SP168 receptor having amino acid sequence SEQ ID NO: 2 (See, *e.g.*, page 3, lines 29-34). These disclosures meet the written description and enablement provisions of 35 USC 112, first paragraph.”

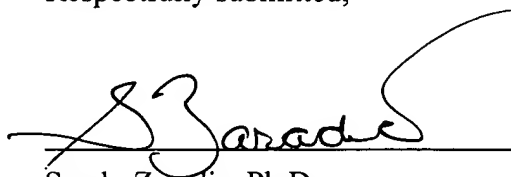
The present claims are directed to a mammalian SP168 receptor defined by the amino acid sequence set forth in SEQ ID NO: 2. Consequently, Applicants believe the present claims meet both the enablement and written description requirements and respectfully request the withdrawal of these rejections.

Claims 1 and 2 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, it was noted that a sequence should be included to more clearly specify the present invention. As the present claims are directed to a mammalian SP168 receptor defined by the amino acid sequence set forth in SEQ ID NO: 2, Applicants believe this rejection is no longer applicable to the present claims and respectfully request withdrawal of this rejection.

CONCLUSION

Applicants respectfully submit that the application is in condition for allowance and request early and favorable action allowing pending Claims 12-18.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Sandy Zaradic', is written over a horizontal line.

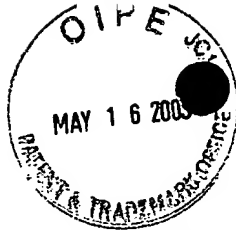
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12. A method for identifying an agonist or an antagonist of a SP168 receptor defined by the amino acid sequence set forth in SEQ ID NO: 2, comprising:
- (a) contacting the SP168 receptor in the presence of a known amount of a labeled SP168 receptor ligand with a sample to be tested for the presence of an agonist or an antagonist of the SP168 receptor; and
 - (b) measuring the amount of the labeled SP168 receptor ligand specifically bound to the SP168 receptor;

whereby the agonist or the antagonist of the SP168 receptor is identified by measuring a difference in binding of the labeled SP168 receptor ligand to the SP168 receptor in the presence of the sample as compared to what would be measured in the absence of the sample.

- 13. The method of claim 12 wherein the SP168 receptor ligand is ADP.
- 14. The method of claim 12 wherein the SP168 receptor ligand is ADP β S.
- 15. The method of claim 12 wherein the SP168 receptor ligand is 2-MeS-ADP.
- 16. The method of claim 12 wherein the SP168 receptor ligand is 2-MeS-ATP.
- 17. The method of claim 12 wherein the SP168 receptor ligand is 2-Cl-ATP.
- 18. The method of claim 12 wherein the SP168 receptor ligand is ATP γ S.



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

On page 1 and 30, please replace the title as follows:

~~G PROTEIN COUPLED RECEPTOR AND METHODS~~

A METHOD FOR IDENTIFYING AN AGONIST OR ANTAGONIST OF A
MAMMALIAN SP168 RECEPTOR

On page 29, please replace the paragraph extending from line 19-29 with the following rewritten paragraph:

The hybridization signals obtained for the SP 168 antisense cRNA probe were relatively consistent in all the normal tissues, although there appeared to be regional differences in the intensity of the signals. In all regions, astrocytes were the only brain cell type which exhibited appreciable hybridization signals. Labeled astrocytes were visible in both the gray and white matter, and accumulations of silver grains were also observed over perivascular astrocytes and astrocytes in subependymal regions. In terms of regional differences, the hybridization signals obtained with the antisense cRNA probe were most intense over astrocytes in temporal cortex, substantia nigra pars reticulata, and amygdala. Moderate signals were ~~abserved~~ observed over thalamic astrocytes, while spinal cord and caudate nucleus contained only weak hybridization signals. In all tissues, only a subpopulation of astrocytes appeared to be labeled.

IN THE CLAIMS

Please cancel claims 1-3.

Please add new claims 12-18.

12. A method for identifying an agonist or an antagonist of a SP168 receptor defined by the amino acid sequence set forth in SEQ ID NO: 2, comprising:

- (a) contacting the SP168 receptor in the presence of a known amount of a labeled SP168 receptor ligand with a sample to be tested for the presence of an agonist or an antagonist of the SP168 receptor; and
- (b) measuring the amount of the labeled SP168 receptor ligand specifically bound to the SP168 receptor;

whereby the agonist or the antagonist of the SP168 receptor is identified by measuring a difference in binding of the labeled SP168 receptor ligand to the SP168 receptor in the presence of the sample as compared to what would be measured in the absence of the sample.

Appendix B

Applicant: Zhang *et al.*; Serial No.: 09/835,922; Filed: April 16, 2001

13. The method of claim 12 wherein the SP168 receptor ligand is ADP.
14. The method of claim 12 wherein the SP168 receptor ligand is ADP β S.
15. The method of claim 12 wherein the SP168 receptor ligand is 2-MeS-ADP.
16. The method of claim 12 wherein the SP168 receptor ligand is 2-MeS-ATP.
17. The method of claim 12 wherein the SP168 receptor ligand is 2-Cl-ATP.
18. The method of claim 12 wherein the SP168 receptor ligand is ATP γ S.